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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/035,596	03/05/98	GUNZBURG W	GSF98-01

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EXAMINER	
CHEN, S	
ART UNIT	**PAPER NUMBER**
1633	10

DATE MAILED: 03/01/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/035,596	Gunzburg et al.
Examiner	**Group Art Unit**
Shin-Lin Chen	1633

☒ Responsive to communication(s) filed on *Dec 13, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1, 2, 4, 5, 9-14, 16-19, 23-33, and 36-73* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 2, 4, 5, 9-14, 16-19, 23-33, and 36-73* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

The amendment filed 12-13-99 (Paper No. 9) has been entered. Claims 3, 6-8, 15, 20-22, 34 and 35 have been canceled. Claims 1, 2, 4, 5, 9-14, 16-19, 23-33 and 36-40 have been amended. Claims 41-73 have been added. Claims 1, 2, 4, 5, 9-14, 16-19, 23-33 and 36-73 are pending in the present application.

Claim Objections

1. A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant's sequence will not be changed. See MPEP § 608.01(n).

Claim 31 depends on claim 36 which is not a claim preceding claim 31. Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2, 10, 11, 18, 19, 31, 32, 44, 45, 55 and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is indefinite because claim 18 depends on a canceled claim 20. Claim 19 depends on claim 18, therefore, claim 19 is also indefinite.

The term "The according" in claim 27 line 1 is vague and renders the claim indefinite. It is unclear what "The according" means.

The term "proximal 445 bp of the WAP promoter" in claims 2, 44 and 55 is vague and renders the claims indefinite. It is unclear what 445 bp of which WAP promoter is intended. Claims 10 and 11 depend on claim 2, thus, claims 10 and 11 are also indefinite.

The term " 320 bp XhoI/XbaI fragment of the WAP promoter" in claims 45 and 56 is vague and renders the claims indefinite. It is unclear what 320 bp XhoI/XbaI fragment of which WAP promoter is intended, because not every WAP promoter has XhoI/XbaI restriction sites.

Claims 31 and 32 recite the limitation "therapeutic gene" in line 1 of each claim. There is insufficient antecedent basis for this limitation in the claim.

4. Claims 41-52 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims fails to teach any steps for delivery of the expression construct containing the heterologous gene and WAP regulatory sequence to a human mammary cell, whereby after

the delivery of the expression construct provides for gene expressing in the human mammary cells.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 23-25 and 37-40 remain rejected and claims 67-73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, and is repeated for the same reasons of record as set forth in the Official action mailed 6-8-99. Applicant's arguments filed 12-13-99 (Paper No. 9) have been fully considered but they are not persuasive.

Claims 67-69 are directed to a pharmaceutical composition comprising a DNA construct comprising a therapeutic gene under the control of a WAP regulatory sequence, a retroviral particle containing said DNA construct or a cell line containing said DNA construct. Claims 70-73 are directed to a method for the treatment of human mammary carcinoma comprising administering to a human a DNA construct comprising a therapeutic gene under the control of a WAP regulatory sequence, a retroviral particle containing said DNA construct, a cell line

containing said DNA construct, or implanting a capsulated cell line containing said DNA construct into a human.

Applicant argues that applicant's data reasonably correlates to expressing a heterologous gene in a human cell and/or treating human mammary carcinoma. Applicant further argues that clinical data is not a requirement of patentability and Shao et al. shows that encapsulated GM-CSF-secreting cells in semi-permeable microcapsules demonstrates the merit of the cell encapsulation system.

This is not found persuasive because the specification of the present application only discloses the construction of vectors pMMTV-BAG and pWAP-BAG containing β-galactosidase gene under the control of a MMTV and a WAP promoter, respectively. The specification shows the expression of β-galactosidase in explanted normal primary human mammary tissue infected with virus containing the vectors set forth above. The specification fails to provide adequate guidance and fails to demonstrate data for the treatment of disorders or diseases of human mammary cells with a DNA construct comprising a therapeutic gene under the control of a MMTV promoter or a WAP promoter, a viral particle containing said DNA construct, cells containing said DNA construct and encapsulated cells, and show the therapeutic effect of said treatment *in vitro* or *in vivo*.

A pharmaceutical composition is a composition which implies *in vivo* applicability such that therapeutic effects against a disease or a disorder are obtained. It is well known in the art that β-galactosidase is a molecular marker and not a therapeutic gene, and such is generally not

considered to be indicative of therapeutic gene expression. The expression of a β-galactosidase in explanted normal primary human mammary tissue infected with vectors pMMTV-BAG and pWAP-BAG is not considered to enable therapeutic gene expression under the control of a MMTV promoter or a WAP promoter, since expression of a marker gene does not correlate with expression of a gene *in vivo*, such that the expression provides for a therapy. It is unclear that expression of a marker gene relates in any way to successful expression of other genes such that a therapy would be obtained.

Furthermore, the state of the art of gene therapy at the time of the invention was unpredictable. The vectors for gene transfer encounter various problems with gene transfer efficiency. Orkin et al. 1995 (X) reported that none of the available vector systems for gene transfer is entirely satisfactory, and many of the perceived advantages of vector systems have not been experimentally validated. Retroviruses infect and integrate only dividing cells. Other problems associated with retroviruses include cumbersome preparation and relatively low titer, size constraints on inserted genes, and the potential for genetic damage due to random integration in the host genome. Adenovirus, Herpesvirus and poxvirus all have the problem of relatively high immunogenicity and complexity of its genome. Adeno-associated virus requires replicating adenovirus to grow and no helper cell line available. Direct administration of DNA or DNA complexes (e.g., liposomes) has disadvantages of lower efficiency of gene transfer (compared with viruses) and the absence of mechanisms for specifically maintaining the introduced DNA within the cell. In terms of the small scale clinical experiment which is referred to as "clinical

trials", the efficacy has not been established for any gene therapy protocol, adverse short term effects related to gene transfer protocols appears to vary, depending on the nature of the virus used as a vector and the patient to which it is administered. Because clinical success is still so limited, it is not possible to exclude longterm adverse effects of gene transfer therapy, the multiple integration events resulting from repeated administration of large doses of retroviruses theoretically pose a risk for leukemic transformation. It is not always possible to extrapolate results from experiments in non-human animals to human studies.

Shao et al. shows that encapsulated cells may be used for prolong delivery of a granulocyte-macrophage colony stimulating factor (GM-CSF) to a tumor site. However, Aebischer et al. reports various problems of encapsulated cells for the treatment of disorder or diseases. Aebischer et al., 1991 (U3) encapsulated PC12 cells in polyelectrolyte-based microcapsules or thermoplastic-based macrocapsules and maintain *in vitro* or transplanted in a rat experimental Parkinson model for 4 weeks. They point out that unencapsulated PC12 cells can lead to the formation of lethal tumors in rats, and do not survive if transplanted into the nervous system of either guinea pigs or mice. The presence of a hydrogel within the microcapsule core possibly impeded cell movement within the capsule, resulting in densely-packed cell aggregates and because their poor mechanical properties, microcapsules are more difficult to implant. Often the implanted microcapsules lost their spherical shape and the retrieval of microcapsules is not possible without significant injury to the brain. In addition, alginate-like materials is found in the vicinity of some microcapsules rasing questions about the

stability of the microcapsules *in vivo*. It is also unclear that if the encapsulated cells will grow within the microcapsule, although the encapsulated cells does not trigger immune response from the host as shown by Aebischer et al. If the cells continue to grow within the microcapsule, it is possible the cells could burst out of microcapsule and trigger immune response. Because the claimed invention encompasses any type of cells containing therapeutic gene under the control of a WAP promoter for the treatment of disease of human mammary cells, administration of cells into immunologically incompatible host, between different species or different individuals in same species for example, would stimulate immune response from the host. Therefore, it is considered to be unpredictable to expect to any degree whether cells or encapsulated cells containing any therapeutic gene would exhibit any therapeutic effect on treating disease of human mammary cells. The specification as filed fails to provide any particular guidance for such.

The quantity of experimentation required to practice the invention as claimed would include isolation of any therapeutic gene which is yet to be identified, determination of the function of said therapeutic gene, generation of a DNA construct or a recombinant viral vector comprising at least one therapeutic gene under transcriptional control of a MMTV or a WAP regulatory sequence, generation of a retroviral particle or cells containing said DNA construct or viral vector, generation of encapsulated cells comprising a core containing said cells, determination of therapeutic effects said DNA construct, viral vector and encapsulated cells on

treating disorders or diseases of human mammary cells including human mammary carcinoma *in vivo*.

In view of the lack of guidance in the specification on how to treat the disorders or diseases of human mammary cells with encapsulated cells containing a construct comprising a therapeutic gene under the control of a MMTV promoter or a WAP promoter and the human unpredictability in art, it would have required undue experimentation for one skilled in the art at the time of the invention to have made a DNA construct or a recombinant viral vector comprising at least one therapeutic gene under transcriptional control of a MMTV or a WAP regulatory sequence, a retroviral particle or cells containing said DNA construct or viral vector, encapsulated cells comprising a core containing said cells to treat disorders or diseases of human mammary cells including human mammary carcinoma, and exhibited therapeutic effect of said treatment *in vivo*. This is particularly true given the nature of the invention, the state of the prior art, the breadth of the claims, the amount of experimentation necessary, the absence of working examples and scarcity of guidance in the specification, and the unpredictable nature of the art.

7. Claims 26-33, 36 and 41-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the expression of a β-galactosidase in normal primary human mammary gland cells infected with the vectors pWAP-BAG or pMMTV-BAG *in vitro*, does not reasonably provide enablement for expression of any gene in any human cell under the control of any WAP promoter derived from any organism other than mouse or a MMTV

promoter. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 26-33 and 36 are directed to a method for the expression of a heterologous gene in a human cell comprising introducing a retroviral vector comprising said gene under the control of a MMTV promoter into the human cell. Claims 27, 31 and 32 specify the heterologous gene is a therapeutic gene such as anti-tumor genes or cytokine genes. Claim 28 specifies the human cell is a mammary cell. Claims 41-52 are directed to a method for the expression of a heterologous gene in a human mammary cell wherein expression of said gene is under the control of a WAP regulatory sequence. Claims 42, 51 and 52 specify the heterologous gene is a therapeutic gene such as anti-tumor genes or cytokine genes. Claim 43 specifies the human mammary cell is a carcinoma cell. Claims 44, 45 and 50 specify the WAP regulatory sequence as recited in the claims.

The specification of the present application discloses expression of a β-galactosidase in normal primary human mammary gland cells *in vitro* infected with the vector pWAP-BAG containing mouse WAP and the vector pMMTV-BAG containing a MMTV promoter.

The specification fails to provide adequate guidance and demonstration as to whether any WAP promoter derived from any organism other than mouse can direct gene expression in human mammary cells, and whether a MMTV promoter can direct gene expression in any human cell type other than normal human mammary gland cells. The specification also fails to teach a

utility for the *in vivo* expression of a β-galactosidase gene under the control of either a MMTV or a WAP promoter. Claims 41-52 encompass any WAP promoter derived from any organism. The specification indicates that "One regulatory element demonstrated to give rise to expression in the pregnant and lactating mouse mammary gland is a small region of the rodent WAP promoter.... It is therefore not predictable that this regulatory element will function at all to direct expression in human mammary cells and/or allow expression in human mammary carcinoma cells" (specification, page 2, lines 15-25). The mechanisms of stimulating downstream gene expression of various WAP promoters derived from different organisms may vary because the core elements of WAP promoter and the cellular interacting transcriptional factors in human cells may vary from species to species. Therefore, it would have been unpredictable whether any WAP promoter other than the mouse WAP promoter will direct gene expression in human mammary cells or in human mammary carcinoma cells.

Claims 26-33 encompass any normal or tumor human cells. Different cell types may have different mechanisms in the transcriptional control of gene expression and the transcriptional machinery in tumor cells is different from that of normal cells. Thus, gene expression via a MMTV promoter in normal human mammary gland cells does not necessarily imply that the MMTV promoter can direct gene expression in other human cell types or in malignant tumor cells. Further, the MMTV promoter is known in the art to be a mammary cell-specific promoter, it is likely that the MMTV promoter can not direct gene expression in any human cell type other than mammary cells.

In view of the lack of guidance and data on whether any WAP promoter other than mouse mammary WAP promoter could direct gene expression in human mammary cells or in human mammary carcinoma cells, and the different transcriptional machinery between different human cell types and between normal and tumor cells, it would have required a skilled person in the art at the time of the invention to have practiced the full scope of the invention. One of skilled person in the art would have to engage in trial and error experimentation to determine whether any WAP promoter other than mouse mammary WAP promoter could direct gene expression in human mammary cells or in human mammary carcinoma cells, and to determine whether the MMTV promoter could direct gene expression in various types of normal human cells and human tumor cells. This is particularly true given the nature of the invention, the state of the prior art, the breadth of the claims, the amount of experimentation necessary, the absence of working examples and scarcity of guidance in the specification, and the unpredictable nature of the art.

The quantity of experimentation required for the invention as claimed includes isolation of putative WAP promoters and downstream genes, identification of WAP promoters derived from various organisms, sequencing of the potential DNA sequences, determination of the WAP promoter function in its native cells, determination of the WAP promoter function to direct gene expression in human mammary cells, construction of an expression vector containing any heterologous gene under the control of a MMTV promoter and determination of the expression of said gene in various types of normal human cells and tumor cells..

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 2, 4, 5, 9-14 and 16-19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Dranoff et al., 1993 (U2) in view of Lefebvre et al., 1991 (V2) and Shao et al., 1994 (X2).

Claims 1, 2, 4, 5, 9-14 and 16 are directed to a retroviral vector comprising a heterologous gene under the control of a MMTV regulatory sequence, a recombinant retroviral particle produced by culturing a packaging cell line harboring said retroviral vector, a retroviral provirus carrying a construct comprising a heterologous gene under the control of a MMTV regulatory sequence, and a packaging cell line harboring said retroviral vector. Claims 2, 4, 5 and 9 specify the MMTV regulatory sequence as recited in the claims. Claim 10 and 11 specify the therapeutic gene as recited in the claims. Claim 17 is directed to an isolated human cell comprising a retroviral provirus as set forth above. Claims 18 and 19 are directed to a capsule encapsulating the packaging cell line, said capsule comprising a porous capsule wall surrounding said packaging cell line.

Dranoff et al. teach subcloning DNA sequences encoding the cytokine such as IL-4, IL-6, γ-IFN, a granulocyte-macrophage colony stimulating factor (GM-CSF), and adhesion molecules

into retroviral vector MFG which contains Moloney murine leukemia virus (Mo-MuLV) long terminal repeat (LTR) and the resulting construct are introduced into CRIP packaging cells to generate recombinant virus which are used to transfect B16 melanoma cells. The transduced B16 cells are inoculated subcutaneously into C57BL/6 mice to monitor the delay of tumor formation associated with the synthesis of cytokine transgene (see e.g. abstract; result, first and second columns). Dranoff et al. does not teach using MMTV promoter for the expression of a gene in a retroviral vector, and a capsule encapsulating the packaging cell line, said capsule comprising a porous capsule wall surrounding said packaging cell line.

Lefebvre et al. reveals the presence of MMTV promoter and the positive and negative regulatory regions upstreams of MMTV promoter (see e.g. abstract) and indicates the hormone responsive element (HRE) (-70-0220) has been well characterized (e.g. introduction). Lefebvre et al. identifies an upstream element, located at the 5' end of the long terminal repeat (LTR), whose enhancer activity is restricted to mammary cells. Shao et al. teaches microcapsules composed of collagen and encapsulated B16-F10 cells transduced with retrovirus containing GM-CSF gene into said microcapsule, and monitor the secretion of GM-CSF in the culture medium (e.g. experimental).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to substitute the Mo-MuLV LTR with MMTV promoter and use with any desired gene for the construction of a recombinant retroviral vector, a recombinant retrovirus containing said retroviral vector, or packaging cells harboring said retroviral vector, and a

capsule encapsulating said packaging cells for the expression of any desired gene product in mammary cells *in vitro or in vivo,* because Mo-MuLV LTR and MMTV promoter both are regulatory sequences derived from LTR and they both have function of directing gene expression. Generation of an isolated human cell comprising a retroviral provirus containing a heterologous gene under the control of a MMTV promoter would have been obvious for a person of ordinary skill at the time of the invention because the claim does not specify that the gene has to be expressed, one could generate an isolated human cell comprising said retroviral provirus just to determine if said gene can be expressed in a human cell.

One having ordinary skill in the art would have been motivated to do this in order to produce a retroviral vector comprising a heterologous gene under the control of a MMTV regulatory sequence, a recombinant retroviral particle produced by culturing a packaging cell line harboring said retroviral vector, a retroviral provirus carrying a construct comprising a heterologous gene under the control of a MMTV regulatory sequence, a packaging cell line harboring said retroviral vector as taught by Dranoff et al., and a capsule encapsulating the packaging cells as taught by Shao et al. for generating a potent, specific and long lasting anti-mammary tumor immunity as taught by Dranoff et al. and Lefebvre et al.

10. Claims 53-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dranoff et al. 1993 (U2) in view of Paleyanda et al., 1994 (W2) and Shao et al., 1994 (X2).

Claims 53-63 are directed to a retroviral vector comprising a heterologous gene under the control of a WAP regulatory sequence, a recombinant retroviral particle produced by culturing a packaging cell line harboring said retroviral vector, a retroviral provirus carrying a construct comprising a heterologous gene under the control of a WAP regulatory sequence, and a packaging cell line harboring said retroviral vector. Claims 55-57 specify the WAP regulatory sequence as recited in the claims. Claims 58 and 59 specify the therapeutic gene as recited in the claims. Claim 64 is directed to an isolated human cell comprising a retroviral provirus as set forth above. Claims 65 and 66 are directed to a capsule encapsulating the packaging cell line, said capsule comprising a porous capsule wall surrounding said packaging cell line. Claim 66 specifies the porous capsule wall consists of a polyelectrolyte complex.

Dranoff et al. teach subcloning DNA sequences encoding the cytokine such as IL-4, IL-6, γ-IFN, a granulocyte-macrophage colony stimulating factor (GM-CSF), and adhesion molecules into retroviral vector MFG which contains Moloney murine leukemia virus (Mo-MuLV) long terminal repeat (LTR) and the resulting construct are introduced into CRIP packaging cells to generate recombinant virus which are used to transfect B16 melanoma cells. The transduced B16 cells are inoculated subcutaneously into C57BL/6 mice to monitor the delay of tumor formation associated with the synthesis of cytokine transgene (see e.g. abstract; result, first and second columns). Dranoff et al. does not teach using WAP promoter for the expression of a gene in a retroviral vector, and a capsule encapsulating the packaging cell line, said capsule comprising a porous capsule wall surrounding said packaging cell line.

Paleyanda et al. teaches constructing a plasmid containing a human protein C (HPC) gene under the control of mouse WAP promoter for making transgenic mouse expressing HPC, and show that the HPC mRNA is detected mainly in the mammary gland (see e.g. abstract). Shao et al. teaches microcapsules composed of collagen as the internal layer and a synthetic polyelectrolyte as the external layer that can be optimized for stability and transport properties. Shao et al. encapsulated B16-F10 cells transduced with retrovirus containing GM-CSF gene into said microcapsule, and monitor the secretion of GM-CSF in the culture medium (e.g. experimental).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to substitute the Mo-MuLV LTR with WAP promoter to combine with any desired gene for the construction of a recombinant retroviral vector, a recombinant retrovirus containing said retroviral vector, or packaging cells harboring said retroviral vector, and a capsule encapsulating said packaging cells for the expression of any desired gene product in mammary cells *in vitro or in vivo,* because Mo-MuLV LTR and WAP promoter both are regulatory sequences and they are similar structurally. Using various region of the WAP LTR would have been obvious for a person of ordinary skill because one would use various WAP promoter regions for the expression of a desired gene product in order to optimize the enhancer or promoter activity of WAP promoter. Furthermore, generation of an isolated human cell comprising a retroviral provirus containing a heterologous gene under the control of a WAP promoter would have been obvious for a person of ordinary skill at the time of the invention

because the claim does not specify that the gene has to be expressed, one could generate an isolated human cell comprising said retroviral provirus just to determine if said gene can be expressed in a human cell.

One having ordinary skill in the art would have been motivated to do this in order to produce a retroviral vector comprising a heterologous gene under the control of an WAP regulatory sequences, a recombinant retroviral particle produced by culturing a packaging cell line harboring said retroviral vector, a retroviral provirus carrying a construct comprising a heterologous gene under the control of a WAP regulatory sequence, a packaging cell line harboring said retroviral vector as taught by Dranoff et al., and a capsule encapsulating the packaging cells as taught by Shao et al. for the study of a method which generates a potent, specific and long lasting anti-mammary tumor immunity as taught by Dranoff et al and Paleyanda et al.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.

DEBORAH J. CLARK
PATENT EXAMINER